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**Identification of Antipsychotic Side Effects with Glassgow Antipsychotic Side-Effect Scale (GASS)****Dita Hasni, Vivinia Rahmi Andika Putri, Mutiara Anissa**

Fakultas Kedokteran, Universitas Baiturrahmah, Padang, Indonesia

ditahasni@fk.unbrah.ac.idDOI: <http://doi.org/10.29080/jhsp.v4i2.268>

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GASS**Abstract**

Schizophrenia is ranked 4th of the top 10 diseases that burden worldwide. If the population of Indonesia reaches 200 million, it estimates that around two million have Schizophrenia. Based on Data from the World Health Organization (WHO), it estimates that around 24 million people worldwide have schizophrenia. The American Psychiatric Association (APA) were reported the incidence of Schizophrenia in the United States is about 1% of the adult population with a total of more than 2 million people. Schizophrenic patients were treated by antipsychotic agents that act to inhibit dopamine receptors, especially D2, and also inhibit adrenergic acetylcholine receptors and serotonin 5-HT2A. It can manifest side effects like extrapyramidal syndrome, amenorrhea, drowsiness, and others. This research aims to the identification of antipsychotic side effects with Glasgow Antipsychotic Side-effect Scale (GASS). 100 schizophrenics in HB. Saanin Mental Hospital were participating in this descriptive study after fulfilling the criteria of inclusion and exclusion. This study used the GASS questionnaire to interview subjects who were signing informed consent and get an explanation about this study. In this study, 92% of subjects reported mild side effects. The frequent complaints were extrapyramidal effects, sedation and CNS effects, anticholinergic effects, and weight gain (93%, 80%, 70% and 70% respectively). We found women complained of the side effects more often (16.38 ± 5.275) than men (12.58 ± 5.484) significantly with the value $P = 0.001$. Gass instruments can use screening antipsychotic side effects. This study concludes the most side effects complaints being extrapyramidal and drowsiness, and women more commonly found side effects than men.

Introduction

Schizophrenia is a psychosis, a mental disorder characterized by abnormal thoughts, hallucinations, delusions (false beliefs), and disruptive work, and social functioning. (1) World Health Organization (WHO) estimates that Schizophrenia affects 20 million people worldwide. It ranks 4 out of 10 major diseases that charge around the world. This mental disorder is associated with disability and interfere in educational and occupational performance (2)

Prevalence of Schizophrenia in the United States, about 1% of the adult population with a total sum of more than 2 million people. (3). According to the Ministry of Health of the Republic of Indonesia in 2018, about 2 million Indonesians suffered Schizophrenia, with a prevalence of 0,7% and the age of sufferers for more than 15 years. If the population of Indonesia is about 200 million, it estimates that about 1,4 million people were suffering Schizophrenia. The national Data on Basic Health Research in 2018 mentions the prevalence of the highest Schizophrenia found in Bali (1,1%), DIY Yogya (1%), NTB (1%), Aceh (0,9%), and West Sumatera (0.9%). (4) A preliminary survey of RSJ Prof. HB Medical Record data. Sa'anin Padang said the number of patients with medication in the year 2011 was 23,870 outpatient, 9,483 (39.73%) Among them are schizophrenia patients and from 1,573 inpatient patients, 812 (51.62%) Among them are schizophrenia patients.

Schizophrenia patients got treatment with antipsychotic drugs. These drugs consist of the typical antipsychotic called by the antipsychotic one generation, and atypical antipsychotics called the second-generation antipsychotics. Typical antipsychotic drugs work inhibiting the dopamine receptor, mainly D2, and also inhibit the muscarinic adrenergic acetylcholine receptors and serotonin 5-HT2A. Both are

atypical antipsychotics, working by inhibiting the receptor, i.e., serotonin 5-HT_{2a} and dopamine, although inhibition on 5-HT_{2A} receptors is more potent than the receptor dopamine. (5) These drugs are indicated for the treatment of psychotic sufferers or other severe psychiatric diseases characterized by agitation and mental disorder. Reserpine and Chlorpromazine are the first drugs that are useful for Schizophrenia. (6)

These drugs can cause adverse reactions since the patient has a subjective or objective complaint due to the use of a drug at a standard dose. The effect can interfere with the quality of life schizophrenic patients and adherence to consuming drugs. Therefore, this research aims to identify complaints of side effects experienced by schizophrenic patients in RSJ HB. Padang Saanin receiving antipsychotic therapy using the Glasgow antipsychotic Side effect Scale (GASS) Questionnaire

Methods

Ethical approval

This research has been approved by the Faculty of Medicine ethics of Baiturrahmah University. The number of Ethic Approval was 047/etik-fkunbrah/03/07/2018. Each participating study subject has signed an informed Consent after reading the research sheet and understanding the explanation given by the researcher.

Research subject and procedure.

One hundred schizophrenic patients were involved in this descriptive study. The subjects were signing informed consent after got an explanation about this research. This research had inclusion and exclusion criteria. The inclusion criteria were a person with Schizophrenia who was diagnosed by a psychiatrist based on DSM IV, the patient got treatment for a minimum of 12 weeks, and a person who willing to participate in research. The exclusion criteria were a person with Schizophrenia in an aggressive condition and is not cooperative. This research was conduct in RSJ HB Saanin Padang after obtaining permission commission of the medical Faculty of Baiturrahmah University. Research subjects are recruited based on a large number of minimal samples using formula

$$n = \frac{Z\alpha^2 P Q}{d^2}$$

$Z\alpha$ = raw deviation alpha • type I error set at 5%, two-way hypothesis, so $Z\alpha = 1.96$.

P = proportions = Proportion of side effects in patients at 42% (based on the manifestation side effect of antipsychotic effect in the previous study)(7)

Q = 1-P = 1-0.42 = 0.58

D = Precision = acceptable prediction Error 10%

By entering the above values in the formula, obtained, we got n = 93 samples, so the minimum number of samples studied was 93.

All participants were interviewed by the data-maker team, who had been trained by a psychiatrist. Interviews using the Glasgow Antipsychotic Side-effect Scale (GASS) questionnaire. (8)

Instruments

All participants have filled in two forms, a demographic form that contains the name, age, education, marital status, diagnosis, and form of the Indonesian version of GASS. The GASS has been translated into Bahasa by a certified translator.

The study uses a GASS version consisting of 22 questions. For any questions side effects of antipsychotic drugs, patients are asked to answer based on what they experienced a week ago (0-Never, 1 – once, 2-a few times, 3-every day). The total score is categorized into 0-21 absent or mild side effects, 22-42 moderate, and 43-63 severe side effects. (8)

The actual question assesses side effects on some organ systems, i.e., Q1-2 for sedation and CNS side effects, Q3-4 for cardiovascular side effects, P5-10 for extrapyramidal side effects, Q11-13 for anticholinergic side effects, Q14 for gastrointestinal side effects, Q15 for the genitourinary side effects, Q16 for DM screening, Q17-21 prolactinaemic side effects, Q22 for weight gain.

Statistical analysis.

Data distribution normality was analyzed using the Kolmogorov-Smirnov test. Categorical Data was presented in frequency and percentage. Comparison of the average value between groups using unpaired T-test and Anova Test.

Results

Demographic characteristics

One hundred people of research subjects who participated in this study have fulfilled the criteria of inclusion and exclusion and complete filling of the questionnaire. Participants consisted of 60 men and 40 women aged 19-82 years. (Average: 37.25, SD = 12.71), the majority not working and unmarried. The demographic characteristics of the research subject are in the table below:

Table 1. Demographic characteristics of research subjects

	N	%
Sex		
Male	60	60,0
Female	40	40,0
Age (mean± SD)	37,25	12,714
Employment Status		
Employed	46	46,0
Unemployed	54	54,0
Mariage		
Single	54	54,0
Married	40	40,0
Divorce	6	6,0
Total	100	100,0

Side effects

In this research the most commonly encountered side effects are: "I felt sleepy during the day" (71%), "I have been gaining weight" (70,0%), "My mouth has been dry" (57.0%), "I have been very thirsty and/or passing urine frequently" (57.0%) and "My movements or walking have been slower up than usual" (55.0%). Absent or mild side effects found in 92 patients (92%), and eight people experienced moderate side effects (8.0%).

Based on the organ systems involved. In this research, reported side effects are often found to be extrapyramidal side effects of 93.0%, sedation, and CNS side effect of 80% as well as weight gain side effects of 71.0%.

Women complained of the side effects more often (16.38 ± 5.275) than men (12.58 ± 5.484) significantly with the value $P = 0.001$. Subjects that do not also work more often complain of side effects (15.41 ± 5.141) compared to the working subject (12.57 ± 5.969). There is no difference in the total score of side effects in single patients (13.52 ± 5.592), married (14.68 ± 5.989) or divorced (14.10 ± 5.690).

Table 2. GASS scale scores

	N	Minimum	Maximum	Mean	Std. Deviation
Total Score	100	2	35	14,10	5,690

Table 3. Most Common Side Effect

No	Side effect	Never n (%)	once n (%)	A few times n (%)	everyday n (%)	Total of complaint n (%)
1	I felt sleepy during the day	29 (29,0)	8(8,0)	20 (20,0)	43 (43,0)	71 (71,0)
2	I felt drugged or like a zombie	82 (82,0)	12 (12,0)	5 (5,0)	1 (1,0)	18 (18,0)
3	I felt dizzy when I stood up and/or have fainted	79 (79,0)	13 (13,0)	7 (7,0)	1(1,0)	21 (21,0)
4	I have felt my heart beating irregularly or unusually fast	68(68,0)	20(20,0)	11(11,0)	1(1,0)	32 (32,0)
5	My muscles have been tense or jerky	47 (47,0)	22 (22,0)	28(28,0)	3 (3,0)	53 (53,0)
6	My hands or arms have been shaky	61 (61,0)	19 (19,0)	15 (15,0)	5 (5,0)	39 (39,0)
7	My legs have felt restless and/or I couldn't sit still	58 (58,0)	17 (17,0)	14 (14,0)	11 (11,0)	42 (42,0)
8	I have been drooling	92 (92,0)	3 (3,0)	3 (3,0)	2 (2,0)	8 (8,0)
9	My movements or walking have been slower than usual	45 (45,0)	20 (20,0)	18 (18,0)	17 (17,0)	55 (55,0)
10	I have had uncontrollable movements of my face or body	79 (79,0)	7 (7,0)	11 (11,0)	3 (3,0)	21 (21,0)
11	My vision has been blurry	60 (60,0)	13 (13,0)	11 (11,0)	16 (16,0)	40 (40,0)
12	My mouth has been dry	43 (43,0)	26 (26,0)	20 (20,0)	11 (11,0)	57 (57,0)
13	I have had difficulty passing urine	85 (85,0)	5 (5,0)	8 (8,0)	2 (2,0)	15 (15,0)
14	I have felt like I am going to be sick or have vomited	88 (88,0)	4 (4,0)	6 (6,0)	2 (2,0)	12 (12,0)
15	I have wet the bed	95 (95,0)	3 (3,0)	2 (2,0)	0	5 (5,0)
16	I have been very thirsty and/or passing urine frequently	43 (43,0)	6 (6,0)	28 (28,0)	23 (23,0)	57 (57,0)
17	The areas around my nipples have been sore and swollen	84 (84,0)	4 (4,0)	9 (9,0)	3 (3,0)	16 (16,0)
18	I have noticed fluid coming from my nipples	97 (97,0)	1 (1,0)	2 (2,0)	0	3 (3,0)

19	I have had problems enjoying sex	81 (81,0)	11 (11,0)	8 (8,0)	0	19 (19,0)
20	Men only: I have had problems getting an erection	39 (65,0)	18 (30%)	3 (5,0)	0	21 (35,0)
Tick yes or no for the last three months		No	Yes	Total of complaint		
		n (%)	n (%)	n (%)		
21	Women only: I have noticed a change in my periods	14 (35,0)	26 (65,0)	26 (65,0)		
22	Men and women: I have been gaining weight	30 (30,0)	70 (70,0)	70 (70,0)		

Table 4. Adverse Effect of Antipsychotics based on Organ System

	N	%
Sedation and CNS side effects		
Yes	80	80,0
No	20	20,0
Cardiovascular side effects		
Yes	46	46,0
No	54	54,0
Extrapyramidal side effects		
Yes	93	93,0
No	7	7,0
Anticholinergic side effects		
Yes	70	70,0
No	30	30,0
Gastrointestinal side effects		
Yes	12	12,0
No	88	88,0
Genitourinary side effect		
Yes	6	6,0
No	94	94,0
Prolactinaemic side effects		
Yes	59	59,0
No	41	41,0
Weight gain side effects		
Yes	70	70,0
No	30	30,0
Total	100	100,0

In the research gained results, complaints of side effects that often arise in antipsychotic users are sedation or drowsiness, extrapyramidal side effects, and increased weight with percentages respectively 80%, 93%, and 70%—shown in table 4.

Table 5. Difference between demographic variables and GASS score

	Mean ± SD	P-value
Sex		
Male	12,58 ± 5,484	0,001
Female	16,38 ± 5,275	
Employment status		
Unemployed	15,41 ± 5,141	0,012
Employed	12,57 ± 5,969	
Married Status		
Single	13,52 ± 5,592	0,517
Married	14,68 ± 5,989	
Divorce	14,10 ± 5,690	

Discussion

In this study, the study subject was recruited the majority of males with an average age of 37.25 ± 12.714, with the majority employment status not working and the most unmarried like the results of this study following the existing theory that the majority of Schizophrenia are men, unmarried and yet to work. This phenomenon occurs because this mental disorder causes the sufferer to struggle to obtain a job and to

run a marriage either as a result of his illness or a negative "stigma" obtained due to mental illness He suffered (2,9,10)

In this study found 92% of research subjects no or mild side-effects, and 8% moderate. It is slightly different from the study that the Serbian who reported 64.2% of his research subjects experienced no or mild side effects, 31.6% moderate, and 4.2% severe side effects. This difference may be due to the overall subject of this study is outpatient, while the revisited research is an outpatient and hospitalization. Schizophrenic people who got therapy in outpatient got administration the drug via oral and the hospitalization patient taking medicine via intravenous. The difference administration of these drugs can affect the severity of side effects. Furthermore, Patients with Schizophrenia who have treated outpatient are usually relatively more stable than inpatients and are more aware of his treatment side effects.

The most side effects complained of patients is the extrapyramidal side effects of 93%, consisting of complaints of muscle twitches, hand tremor, drooling. The leg had felt restless, walking slower than usual and can not control movement in the face or body amounting to 53.0%, 39.0%, 42.0%, 8.0%, 55.0%, and 21.0%. These findings were higher than previous studies that reported the incidence of extrapyramidal side effects by 41.1% in Serbia. This phenomenon caused the entire subject research only gets clozapine. (11)

The blockade of the dopamine D2 receptor is the primary mechanism of antipsychotic treatment. Inhibition of these receptors in the mesolimbic system area will provide psychological effects and correct performance disorders. The dopamine D2 receptors are also found in the area of the region, the Basal Ganglia, which plays a role in motor movements. The blockade of D2 receptors in this area will cause extrapyramidal disorders such as Parkinsonism, Dyskinesia, tardive dyskinesia, etc. (5,12)

His other complaints are quite often drowsiness of 71%, and his 43% feel sleepy every day. Sedation is a side effect that is often the reason for the end of the drug in schizophrenia patients (Legge et al., 2016). This complaint belongs to the category of sedation and CNS side effects. The research was reported at 80%. This drowsiness arises from the blockade of histamine receptors due to the use of antipsychotic drugs. (13)

In addition to feeling sleepy, complaints often feel thirsty or frequent urination is one of the complaints that often found in this research (more than 50%). Often feeling thirsty and urination at this research is slightly lower than the research of Ignjatović Ristić et al., 2018. 57% vs. 62%. Complaints often feel thirsty, and urination on this research becomes essential to evaluate patients against diabetes mellitus. It is necessary to watch out because this typical or atypical antipsychotic drug works primarily on inhibition of dopamine D2 and D3 receptors. These receptors are also found in the cell β pancreas and have a role in glucose regulation to inhibit the release of insulin. Inhibition of these receptors by antipsychotic drugs will increase the release of insulin. If it occurs chronically, it will cause insulin resistance similar to hyperinsulinemia in the condition of Diabetes mellitus type 2. (14,15)

Another complaint that is often reported in this research is dry mouth (more than 50%). Dry mouth is one of the symptoms of the anticholinergic effects occurring due to the inhibition of muscarinic receptors on the use of antipsychotics. (Lally & MacCabe, 2015) In this study reported complaints of anticholinergic side effects amounted to 70.0%, with details of blurred eyes 40.0%, dry mouth 57%, and urine retention 15.0%). The findings were not much different from the prior research that reported a dry mouth complaint of 52.6% and a blurred vision of 43.2%. (11)

Complaints of a weight gain are also quite often found in this study by 70.0%; this complaint is slightly higher than its research of 42.0%. This complaint is associated with a leptin signaling mechanism that is interrupted due to the use of antipsychotics. This phenomenon results in an increase in appetite in patients who get antipsychotics, which tends to weight gain. (14,16)

This study reported that female patients more often reported side effects than male patients. This is because women tend to be more often overdose than men. After all, the pharmacokinetics of women has a smaller distribution volume, higher free drug fraction, and a slower elimination process. This mechanism will result in higher plasma levels of the drug in women than men. (17,18).

This study also reported that patients who did not have a job tend to report more often side effects than patients who worked. This phenomenon is due to patients who are not working tend to be more concerned about his body condition to the side effects he suffered because his daily activities are not distracted by doing the work.

Conclusion

This research concludes that Gass instruments can use screening antipsychotic side effects, and The commonly reported side effects in this study are the mild effects, and most complaints are extrapyramidal effects, sedation, and weight gain effects.

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